REMARKS

Claims 1, 24-28 and 33-37 are pending. No new matter has been added by way of the present submission. For instance, claim 1 has been amended to more specifically define the invention in terms of the substitutions disclosed in the specification and examples. Withdrawn claims 20-23 and claims 29-32 have been cancelled. New claims 33-37 are supported by the present specification as well as the original claims. Thus, no new matter has been added.

In view of the following remarks, Applicant respectfully requests that the Examiner withdraw all rejections and allow the currently pending claims.

Issues under 35 U.S.C. § 112, first paragraph

The Examiner has rejected claims 1 and 24-32 under 35 U.S.C. § 112, first paragraph for the reasons recited at pages 2-7 of the outstanding Office Action. The Examiner has presented grounds of rejection based upon "written description" as well as "enablement." Applicant respectfully traverses each rejection and will deal with them separately below.

There exists sufficient written description for the presently claimed subject matter.

Applicant respectfully submits that the presently pending claims, which require specific substitutions at specific locations, fully satisfy the written description requirements of 35 U.S.C. § 112, first paragraph. Indeed, the present claims define subject matter which was described in the specification in such as way as to reasonably convey to one skilled in the art that the Applicant, at the time the application was filed, had possession of the claimed invention.

The Examiner asserts that the present claims define "any" water soluble mutant pyrroloquinoline quinone glucose dehydrogenase (PQQGDH), wherein the PQQGDH comprises

any mutant PQQGDH having one or more amino acid residue substitutions in SEQ ID NO:1. Thus, the Examiner asserts that the claims encompass an unlimited number of substitutions in SEQ ID NO:1. Applicant submits that the Examiner must properly construe the present claims with deference to knowledge in the art and the present specification.

As admitted by the Examiner, the present specification discloses the structure of SEQ ID NO:1. Further, the present specification includes specific description of the particular substitutions subject to the present claims, for instance, see claim 1 above. Thus, it is clear to those of skill in the art that Applicant possessed these specific substitutions. However, those of skill in the art would understand that Applicant possessed much more than only the specifically disclosed substitutions.

In fact, those of skill would understand that Applicant possessed the specifically disclosed substitutions or combination of substitutions in any PQQGDH. This does not mean that the PQQGDH can be modified such that it is no longer a PQQGDH. Applicant ensured this by including the limitation "mutant water-soluble glucose dehydrogenase having pyrroloquinoline quinone as a coenzyme." Thus, the claimed PQQGDH must always remain a PQQGDH. Moreover, this claimed PQQDGH must contain one of the specific substitutions. However, there is no evidence that those of skill in the art would understand that Applicant did not possess other PQQGDHs so long as one of the specific substitutions is present. There is also no evidence that other substitutions would cause the molecule to no longer be a PQQGDH. And, even if a non-PQQGDH molecule resulted, this would not be encompassed by the present claims in view of the requirement for a "mutant water-soluble glucose dehydrogenase having pyrroloquinoline quinone as a coenzyme."

Additionally, the Examiner must take into consideration the fact that the present specification contains detailed disclosure concerning not only the particular substitutions, but also particular amino acid residue "ranges" that can be modified. For instance, at page 3, second full paragraph, the present specification describes the fact that modified PQQGDHs may contain one or more amino acid residue substitutions in the region of 186-206 or in an equivalent region. It is therefore evident that the specification provides disclosure of both the structural and functional aspects of the present PQQGDHs.

Thus, Applicant has described, and was in fact in possession of the particularly claimed genus. Moreover, Applicant provided the disclosure of a representative number of species within this genus. A specification may, within the meaning of 35 U.S.C. § 112, contain a written description of a broadly claimed invention without describing all species that the claim encompasses. Utter v. Hiraga, 845 F.2d 993, 6 USPQ2d 1709, 1714 (Fed. Cir. 1988). In Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398 (Fed. Cir. 1997), the Federal Circuit recognized that "in claims involving chemical materials, generic formulae usually indicate with specificity what the generic claims encompass." However, the Federal Circuit also acknowledged in Lilly its holding in Utter v. Hiraga, 845 F.2d 993, 998-999, 6 USPQ2d 1709 (Fed. Cir. 1988), that "[a] specification may, within the meaning of § 112 paragraph 1, contain a written description of a broadly claimed invention without describing all species that claim encompasses." While the Federal Circuit declined to extend Utter in Lilly to claims involving genetic material, it did not abandon its holding for chemical materials noting that in the case of generic formulae, "[o]ne skilled in the art can distinguish such a formula from

others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate description of the claimed genus." Lilly, 119 F.3d at 1568.

The main reason for this distinction is that generally, claiming all DNAs that achieve a **result** without defining what means will do so is not in compliance with the description requirement; it is an attempt to preempt the future before it has arrived. However, the present facts are distinct from those of Lilly and its progeny cases. In the present instance, the structure of the PQQGDH is known. Also, PQQGDHs and their respective coding and amino acid sequences are known in the art. What is new in the present invention is the specifically claimed substitutions, not the molecule itself.

In Enzo Biochem Inc. v. Gen-Probe Inc., 296 F.3d 1315, 63 USPQ2d 1609 (Fed. Cir. 2002), the claimed nucleotides were characterized in the specification only by biological activity or function. Although they had been actually reduced to practice and bacterial hosts containing the material had been deposited at the American Type Culture Collection, the nucleotides had not been sequenced and therefore no structural description appeared in the specification. As a matter of first impression, the court held reference in the specification to a deposit in a public depository, which makes its contents accessible to the public when it is not otherwise available in written form, constitutes an adequate description of the deposited material sufficient to comply with the written description requirement of § 112 paragraph 1. However, the claims in question were not limited to the deposited materials, but also covered subsequences and mutated variants of those materials. Accordingly, the court remanded for a determination of whether, as a matter of fact, "a person of skill in the art would glean from the written description, including information obtainable from the deposits of the claimed sequences, subsequences, mutated

variants, and mixtures sufficient to demonstrate possession of the generic scope of the claims." 63 USPQ2d at 1615. Broader genus claims were also remanded for a determination of whether one of skill in the art would find the generically claimed sequences described on the basis of a disclosure of the involved function and an accessible structure.

In the present instance, the case of Enzo can be distinguished. As noted above, the structure of the PQQGDH is known. Also, PQQGDHs and their respective coding and amino acid sequences are known in the art. What is new in the present invention is the specifically claimed substitutions, not the molecule itself. Also, in Enzo, the Court clarified that Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure.

In fact, all of the recent written description cases can be distinguished. In Lilly, 119 F.3d at 1567, the cDNA for human insulin had never been characterized. In Enzo, 296 F.3d at 1326, the court reaffirmed that deposit of a physical sample may replace words when description is beyond present scientific capability. In Amgen Inc. v. Hoechst Marion Roussel, Inc., 314 F.3d 1313, 1332, 65 USPQ2d 1385 (Fed. Cir. 2003) the court explained further that the written description requirement may be satisfied "if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure." These evolving principles were applied in Noelle v. Lederman, 355 F.3d 1343, 1349, 69 USPQ2d 1508 (Fed. Cir. 2004), where the court affirmed that the human antibody there at issue was not adequately described by the structure and function of the mouse antigen; and in University of Rochester v. G.D. Searle & Co., 358 F.3d 916, 925-26 69 USPQ2d 1886 (Fed. Cir. 2004), where the court affirmed that the

description of the COX-2 enzyme did not serve to describe unknown compounds capable of selectively inhibiting the enzyme.

Although the Examiner asserts that a representative number of species has not been disclosed, Applicant disagrees. The genus claimed in the present invention is limited to specific PQQGDHs have particular substitutions. True, other substitutions could be present, so long as a PQQGDH is still present. However, this does not mean that the requisite structure has not been disclosed. Therefore, Applicant submits that those of skill in the art would understand that Applicant was in possession of the claimed subject matter at the time of filing. Based upon the above, Applicant respectfully requests that the Examiner withdraw this rejection based upon 35 U.S.C. § 112, first paragraph, written description.

There exists sufficient written description for the presently claimed subject matter.

Applicant respectfully submits that the presently pending claims, which require specific substitutions at specific locations, fully satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph. Indeed, the present claims define subject matter which those of skill in the art are able to make and use without undue experimentation.

The enablement requirement of 35 U.S.C. § 112, first paragraph requires that the specification teach one of ordinary skill in the art how to make and use the claimed invention without undue experimentation. The determination of whether an invention requires undue experimentation is not based on a single factor, but is rather a conclusion reached by weighing many factors. The dominant factors have been summarized as follows:

1. the quantity of experimentation necessary (time and expense);

2. the amount of direction or guidelines presented in the application;

3. the presence or absence of working examples of the invention in the application;

4. the nature of the invention;

5. the state of the prior art;

6. the predictability or unpredictability in the art; and

7. the breadth of the claimed invention.

In re Wands, 858 F.2d 731, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

However, the fact that experimentation may be complex does not necessarily make it undue if a person skilled in the art typically engages in such experimentation. In re Borkowski, 422 F.2d 904, 164 USPQ 642, 645 (CCPA 1970). The test for enablement is not whether experimentation is necessary, but rather the test is if experimentation is necessary, is it undue? In re Angstadt, 537 F.2d 498, 190 USPQ 214, 219 (CCPA 1976).

The Examiner again points out that although the claims require specific substitutions, they are sufficiently broad as to encompass any substitution in any location of SEQ ID NO:1. Applicant disagrees. As already discussed above, those of skill would understand that Applicant possessed the specifically disclosed substitutions or combination of substitutions in any PQQGDH. This does not mean that the PQQGDH can be modified such that it is no longer a PQQGDH. Applicant ensured this by including the limitation "mutant water-soluble glucose dehydrogenase having pyrroloquinoline quinone as a coenzyme." Thus, the claimed PQQGDH must always remain a PQQGDH. Moreover, this claimed PQQDGH must contain one of the specific substitutions.

However, there is no evidence that those of skill in the art would not be able to make other PQQGDHs so long as one of the specific substitutions is present. It is understood that the preparation of other PQQGDHs containing the present substitutions and other substitutions are within the skill in the art. This knowledge exists even apart from the detailed description provided in the present specification. Also, the molecule is well defined as is the use thereof. The present specification contains disclosure of particular testing methods for activity, see pages 9-11.

The Examiner attempts to argue that "undue experimentation" would be necessary since it is not routine to screen for multiple substitutions or multiple modifications. Thus, labs generally do not undertake such a search. However, even if this is hypothetically correct and such screening is not routinely practiced, if one wanted to prepare such additional modifications, the experimentation to do so would be routine. The test is therefore not whether such screening is routinely undertaken, but rather whether the screening, when undertaken, involves routine methods. In fact, Applicant has indicated that if such modifications are desired, those of skill in the art are able to compare the secondary structures of proteins predicted from the primary structures of the enzymes, see page 8, 3rd full paragraph. This technique would allow for targeting of susceptible regions to modify.

As such, Applicant submits that those of skill in the art are fully able to make and use the presently claimed invention without undue experimentation. The Examiner is thus requested to withdraw this enablement rejection.

Issues under 35 U.S.C. § 102(b)

The Examiner has rejected claims 1, 24-27, 30 and 32 under 35 U.S.C. § 102(b) as being anticipated by Kratzsch et al., WO 02/34919.

The Examiner has also rejected claims 1, 24-27, 30 and 32 under 35 U.S.C. § 102(b) as being anticipated by Sode et al., WO 00/61730.

Lastly, the Examiner has rejected claims 1, 24-27, 30 and 32 under 35 U.S.C. § 102(b) as being anticipated by Sode et al., WO 00/66774.

Applicant respectfully submits that the cited art above fails to suggest or disclose the presently claimed subject matter. For instance, independent claim 1 requires an isolated mutant water-soluble glucose dehydrogenase having pyrroloquinoline quinone as a coenzyme, wherein said mutant is a mutant of a glucose dehydrogenase comprising the amino acid sequence of SEQ ID NO:1, and wherein said mutant consists of an amino acid substitution selected from the group consisting of:

(1) glutamine at position 192 (168th glutamine of SEQ ID NO:1) is substituted with glycine, glutamic acid, leucine, phenylalanine, serine or aspartic acid in SEQ ID NO:1, optionally combined with (a) a substitution wherein aspartate at position 167 (143rd aspartate of SEQ ID NO:1) is substituted with glutamic acid in SEQ ID NO:1 or (b) a substitution wherein asparagine at position 452 (428th asparagine of SEQ ID NO:1) is substituted with threonine in SEQ ID NO:1;

(2) leucine at position 193 (169th leucine of SEQ ID NO:1) is substituted with alanine, glycine, methionine, tryptophan or lysine in SEQ ID NO:1, optionally combined with (a) a substitution wherein aspartate at position 167 (143rd aspartate of SEQ ID NO:1) is substituted

with glutamic acid in SEQ ID NO:1 or (b) a substitution wherein asparagine at position 452 (428th asparagine of SEQ ID NO:1) is substituted with threonine in SEQ ID NO:1; and

(3) aspartate at position 167 (143rd aspartate of SEQ ID NO:1) is substituted with glutamic acid in SEQ ID NO:1, and asparagine at position 452 (428th asparagine of SEQ ID NO:1) is substituted with threonine in SEQ ID NO:1.

The particular substitutions recited in the present claims are absent from the cited art. Therefore, there exists no anticipation. Reconsideration and withdrawal of these rejections are therefore respectfully requested.

In view of the above, Applicant respectfully submits that the present claims are in condition for allowance. Therefore, the Examiner is requested to withdraw all rejections and allow the currently pending claims.

If the Examiner has any questions or comments, please contact Craig A. McRobbie, Registration No 42,874 at the offices of Birch, Stewart, Kolasch & Birch, LLP.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to our Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under § 1.17; particularly, extension of time fees.

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Respectfully submitted,

By #42,874

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